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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/551,771	03/07/2006	Olivier Besnard	0540-1038	5725

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EXAMINER

YOUNG, HUGH PARKER

ART UNIT	PAPER NUMBER
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1654

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/551,771

Applicant(s)

BESNARD ET AL.

Examiner

Hugh P. Young

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 March 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 8 is/are rejected.
- 7) ☒ Claim(s) 4 - 7 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

This is the first Office Action on the application, 10/551,771, of Besnard et al. There are eight claims pending and all eight claims are under consideration.

OBJECTIONS TO THE CLAIMS

1. Claim 4 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may depend from multiple claims only in the alternative form. Claim 4 is so worded as to depend from more than one of claims 1 – 3. See MPEP § 608.01(n). Accordingly, claim 4 has not been further treated on the merits.
2. Claims 5 - 7 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim may depend from multiple claims only in the alternative form. Claims 5 – 7 are depended from claim 4, which is an improperly constructed multiply dependent claim. See MPEP § 608.01(n). Accordingly, claims 5 – 7 have not been further treated on the merits.

Information Disclosure Statement

3. Reference : Chakrabartty A., et al (1995): "Stability of alpha-helices" in: Advances in Protein Chemistry, Academic Press, New York. Vol. 46:141-176, was not considered because a copy was not provided by the applicant.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

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Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claim 8 is rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The claim is for a method of using the invention of claim 1 but does not recite any active step(s).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 1, 2, 3 and 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case applicant claims oligopeptides that will form spiral structures that are essential to the functioning of the invention. It is known in the art that formation of spiral structures by amino acid sequences is dependent on the actual sequence of the peptide, especially the nature and orientation of the individual peptides, as well as being heavily dependent on the environmental context in which the peptide is formed or present.

In this regard, the application disclosure and claims have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2d 1400 (Fed. Cir., 1988) as to

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undue experimentation. Each factor is addressed below on the basis of comparison of the disclosure, the claims and the state of the prior art in the assessment of undue experimentation. The factors follow:

1. *the nature of the invention*: The invention is a set of oligopeptides belonging to a relatively new class of peptides, the peptaibols, which are derived from fungi.

2. *the breadth of the claims*: The oligopeptides, as claimed, are defined very broadly so as to encompass many possible products. This is further compounded by the lack of specificity in claiming what is or is not included as substituents in side chains.

3. *the predictability or unpredictability of the art*: Spiral, or helix, formation of peptides is known in the art to be unpredictable, varying with the character of the monomers comprising the peptide sequence, conditions of temperature and solvation in which they were formed, and the milieu in which they are kept or used after they are made. Berendsen (H. J. C. Berendsen; "A glimpse of the holy grail?" *Science* (1998) 282:642-643) states "The prediction of the native conformation of a protein of known amino acid sequence is one of the great open questions in molecular biology and one of the most demanding challenges in the new field of bioinformatics." (page 642).

Jones (D. T. Jones, "A practical guide to protein structure prediction," in *Protein Structure Prediction; Methods and Protocols*; (2000), D. Webster, eds.) states that "The protein-folding problem is one of the greatest remaining challenges in structural molecular biology" because of both the innate complexity and variability of the molecules themselves as well as the practical problems with the analytical methods used to determine structure.

Ngo (Ngo J. T., et al. "Computational Complexity..." in *The Protein Folding Problem and Tertiary Structure Prediction*. (1994). K. Merz, Jr. and S. LeGrand, Eds., pages 492-495) teaches that "it is not known whether there exists an efficient algorithm for predicting the structure of a given protein from its amino acid sequence alone. Decades of research have failed to produce such an algorithm, yet Nature seems to solve the problem." (page 492).

Padmanabhan (Padmanabhan S., et al. *Nature* (1990) 344:268-270) teaches that "... the helix-forming tendency of a particular amino acid depends on the sequence context in which it occurs" (Abstract) and that "helix-forming tendency varies widely among the 20 amino acids, and substitution of a single residue can have a marked effect on helix stability..." (page 270).

4. *the amount of direction or guidance presented*: The amount of guidance provided in the disclosure is sufficient to produce a small array of products as in applicants' list on page 15 of the Specification. Compounds 8 – 15, as disclosed, are but examples of polyalanine with chain lengths of from 3 to 10 alanine residues. Beyond this no particular examples are provided. No guidance is provided as to how the various possible main backbone or sidechain moieties are to be chosen, and what if any change in synthesis, product obtained, or effect on the characteristics or uses of the products is provided. No guidance is provided on how one may extrapolate from the results they present to the more general forms as claimed.

Berendsen (*Science*, 1998), Ngo (*The Protein Folding Problem and Tertiary Structure Prediction*, 1994) and Padmanabhan (*Nature*, 1990), as cited supra, teach

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that the variability of products obtained and their behavior in solution is both variable and unpredictable.

5. *the presence or absence of working examples*: The working examples disclosed, the series of short-chain polyalanine oligopeptides, is one of the simpler embodiments of the invention as claimed, and there is no rationale provided as to why these embodiments are preferred over any others. The series of working examples disclosed is so narrow as to not reasonably represent the extent and amount of variability present in such a broad genus. The working examples of efficacy by changing peroxidase activity in plant tissue are directed to unspecified biochemical and enzymatic actions in tissue homogenates, not whole-plant effects that can be shown to be imparting disease resistance in the real world. The enzyme activity itself, although recited by applicant as being fundamental to host-plant response to infection or invasion, is a broadly distributed enzyme action with many biological systems showing activity in varied contexts.

6. *the quantity of experimentation necessary*: In light of items 1 – 5 above, it can be seen that an undue amount of experimentation will be required in order to practice the invention as disclosed. The genus of oligopeptides claimed is very broad, with no guidance as to choose, a priori, from among them and pick out those which can be both reliably produced and then be expected to have any positive or consistent effect on the disease resistance of target host plants.

7. *the state of the prior art*: The art of peptide synthesis and conformation is well known and within its broad scope there are citations (Berendsen (*Science* 1998), Ngo

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(*The Protein Folding Problem and Tertiary Structure Prediction*, 1994) and Padmanabhan (*Nature*, 1990) that illuminate the degree of unpredictability within the art. Jones (D. T. Jones, "A practical guide to protein structure prediction," in *Protein Structure Prediction; Methods and Protocols*; (2000), D. Webster, eds.) state that "The protein-folding problem is one of the greatest remaining challenges in structural molecular biology" because of both the innate complexity and variability of the molecules themselves as well as the practical problems with the analytical methods used to determine structure. Furthermore, the area within the art in which the inventors have claimed their invention, peptaibols, is relatively new and not thoroughly studied in either depth or breadth. In this respect the practitioners of this art have made few assertions that would cause one to conclude that the lack of predictability found in the broader art of peptides is much ameliorated by knowledge of peptaibols. Indeed, the relative novelty of peptaibols makes any prediction of the outcome of either a synthetic process or a use of a product once obtained as yet unpredictable.

8. *the relative skill of those skilled in the art:* In view of the discussion of each of the preceding seven factors the level of skill in this art is high and is at least that of a synthetic organic chemist with an advanced degree with several years of experience in the art, plus experience in the agricultural and horticultural art in the field of plant pathology. As the cited art would point to, even with a level of skill in the art which is very high, given that predictability of the results is not invariable.

In consideration of each of factors 1 - 8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by

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the present application disclosure, examples, teaching, and guidance presented.

Absent factual data to the contrary, the amount and level of experimentation needed is undue.

8. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim is for a method of using the composition of claim 1 but does not recite any active step(s) for actually using it. The claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Use of the composition of prior claims is claimed without disclosing any active method steps. Claim 8 states that the compositions are to have an effect "when applied" but give no active steps for this application, including no definition of what means or mode will be used to apply them, in what form the composition will be in order to be applied, and at what time or stage or in what condition either the host plant being protected or the pathogen being addressed may be in at the time of application. Furthermore, applicant claims that the use of the invention will have "the effect of reducing" harmful organisms or host-plant responses without defining what is meant by "reducing".

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claim 1, 2, 3, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Please note: Claim 8 has been interpreted as a product with an intended use for the purpose of this rejection.

Regarding claim 1, the phrase "and/or" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 2 recites the word "can" when claiming that R1 and R2 "can be identical," which is a conditional limitation that is made without stating the conditions under which R1 and R2 may or may not be identical. See MPEP § 2173.05(d).

Claims 2 and 3 recite the limitation "R = H" in the third line of text, without a prior definition or recitation of where "R" is, either in text or in the structural diagrams provided. There is insufficient antecedent basis for this limitation in the claim. See MPEP § 2173.05(d).

In claim 8, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Regarding claim 8, the phrase "the attack of" renders the claim indefinite because it is unclear what is meant by "attack". It is unclear as to whether this implies simple contact between host and pathogen, penetration of the host by the pathogen, or any more advanced stage or stages of invasion, infestation or infection. It is further

unclear as to whether any physiological disease response by the host plant is encompassed by the claim. See MPEP § 2173.05(d).

Regarding claim 8, the word "particularly" renders the claim indefinite because the claim includes elements not actually disclosed (those encompassed by "particularly"), thereby rendering the scope of the claim unascertainable. See MPEP § 2173.05(d).

In further regard to claim 8, use of the word "with" renders the claim indefinite because it is unclear as to whether the applicant means "with" or "by" in reference to what may be a pathogenic agent(s) and what may be co-hosts or symbionts in the portions of claim 8 reciting "lawns and horticulture" and "oil producers." See MPEP § 2173.05(d).

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1, 3, and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,283,283, which discloses and claims (column 7; claims 1, 2 and 3) polypeptides including polyalanine, polyleucine, polyglutamine and other poly(alpha-amino acids) . Patent No. 5,283,283 also teaches that the polypeptides claimed therein occur in the alpha-helix configuration (column 6, lines 63-66; column 7, claims 1 and 4), and further teaches other aspects of the sizes (column 5, lines 54-63; column 6, lines 30-39) and modifications of the peptides and component amino acids (column 5, lines 18-32). In the instant application, claims 1, 3, and 8 claim a broad set of peptides which

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encompass polypeptide polyalanine and others, and polyalanines are disclosed in the table on page 15 of the instant Specification, which are anticipated by claims 1, 2, and 3 of No. 5,283,283. In the instant application applicants further claim a spiral or helical structure, which is also taught by No. 5,283,283 in claims 1 and 4 (column 7) and the disclosure (lines 63-66, column 6). Aspects of the instant application's claims directed to overall size, composition of side chains, and other modifications of the amino acids and peptides are anticipated by No. 5,283,283 in the disclosure, column 5, lines 54-63; column 6, lines 30-39, and column 5, lines 18-32.

SUMMARY

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hugh P. Young whose telephone number is (571)-272-4988. The examiner can normally be reached on 8:00 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hugh P. Young Ph.D.

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B. DELL CHISM
PATENT EXAMINER